UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,708	01/14/2004	Derek O' Hagan	PP-19768.002	3852

27476 7590 08/04/2010

NOVARTIS VACCINES AND DIAGNOSTICS INC.
INTELLECTUAL PROPERTY- X100B
P.O. BOX 8097
Emeryville, CA 94662-8097

EXAMINER	
POPA, ILEANA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/757,708	O' HAGAN ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28, 32-39, 42-48, 52, 54-64, 69, and 72-101* is/are pending in the application.

4a) Of the above claim(s) *4,7,11,14,19-22,24,25,58-60,62,72-75,84 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 1-3,5,6,8-10,12,13,15-18,23,26-28,32-39,42-48,52,54-57,61,63,64,69,76-83 and 86-101.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/01/2010 has been entered.

Claims 29-31, 40, 41, 49-51, 53, 65-68, 70, and 71 have been cancelled.

Claims 4, 7, 11, 14, 19-22, 24, 25, 58-60, 62, 72-75, 84, and 85 have been withdrawn.

Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 32-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76-83, and 86-101 are under examination.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude"

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 32-39, 42-48, 52, 54, 55, 61, 69, 76-83, and 90-101 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-19, 24-26, and 35-40 of U.S. Patent No. 6,884,435. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

The instant claims are drawn to **(i)** microparticles comprising a biodegradable polymer, a cationic lipid, and a first polynucleotide-containing species adsorbed on the surface of the microparticles, wherein the first polynucleotide species constitute at least 5% of the total weight of the microparticles, the cationic surfactant is cetyltrimethylammonium bromide (CTAB), the biodegradable polymer is poly(lactide-co-glycolide) (PLG), the first polynucleotide-containing species encodes for an antigen derived from a pathogenic organism such as HIV, the microparticles further comprise an immunological adjuvant such as CpG ; the microparticles can contain 01-10 wt% cationic surfactant or additional microparticles comprising entrapped or adsorbed immunological adjuvants (claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 34-37, 43, 69, 76-79, and 90, 91, and 96-100), **(ii)** a method of producing the microparticles by obtaining a w/o/w emulsion comprising the polymer and the surfactant, removing the

organic solvent from the solution and adsorbing the first polynucleotide-containing species to the microparticles (claims 52, 54, 55, 92-95, and 101), **(iii)** a method of delivering a therapeutic amount of polynucleotide to a host animal (claim 38), and **(iv)** a method of stimulating an immune response, wherein the immune response comprises a CTL immune response (claims 39, 42, 44-48).

The patent claims recite **(i)** a microparticle comprising a polymer such as PLG, a cationic detergent such as CTAB, and an antigen comprising a polynucleotide such as plasmid (example 7 discloses that the plasmid is pCMV) adsorbed on the surface of the microparticle, wherein the polynucleotide encodes for an antigen derived from a pathogenic organism such as HIV and wherein the microparticle is formed in the presence of the detergent and then exposed to the polynucleotide (the specification defines that a w/o/w solvent evaporation system can be used to form the microparticles, see column 13, lines 10-39); the microparticles further comprise CpG as an immunological adjuvant (claims 1, 5-13, 16, 17, 19, 20, 24-26, 35-37) and **(ii)** a method for raising an immune response by administering the microparticles to a vertebrate animal (the specification discloses that the intent of delivery is to use the particle as a vaccine to elicit an immune response in a vertebrate and to treat a disease, see column 4, lines 3-30; additionally the specification defines that a vertebrate can be a human, column 8, lines 45-52) (claims 38-40). The specification discloses that the polynucleotide can constitute 5% or 0.1 to 10% of the total weight of the microparticle (column 14, lines 6-10) and that the microparticles comprise 0.1 to 10% or 0.5 to 2 % cationic surfactant (column 13, lines 30-37). The specification also discloses that the

cationic surfactant is not removed after the formation of the microparticles (column 13, lines 10-39). With respect to the limitation of the adjuvant being adsorbed on the surface of the microparticle, the specification discloses that adjuvants can be used to enhance the immunogenicity of the microparticles and that the adjuvants can be adsorbed on the microparticles (column 14, lines 36-51). With respect to the limitation recited in claim 3, the specification discloses that the microparticles have a diameter of about 200 nm to about 30 μm that includes the range recited by claim 3 (column 5, lines 1-10). With respect to the limitation of the polynucleotide constituting 10-20% of the total microparticle weight (the instant claims 27, 28, 91, and 93), it would have been obvious to one of skill in the art to adjust the amount of delivered polynucleotide according to particular needs by varying the amount of adsorbed polynucleotide. It is routine in the art to vary the relative ratios of the microparticle components and test for the combinations that result in better activity.

Thus, the patent claims and the instant claim are obvious variants.

The applicant's arguments are not new and were previously addressed.

4. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26, 28, 32-37, 54, 55, 61, 69, 76-83, and 90-101 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 11, 30, 31, 36, 37, 40, 43, 45-47, 58, 59, 71, and 79 of the U.S. Application No. 11/113,861. Although the conflicting

claims are not identical, they are not patentably distinct from each other because they are obvious variants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are drawn to **(i)** microparticles comprising a biodegradable polymer, a cationic lipid, and a first polynucleotide-containing species adsorbed on the surface of the microparticles, wherein the first polynucleotide species constitute at least 5% of the total weight of the microparticles, the cationic surfactant is cetyltrimethylammonium bromide (CTAB), the biodegradable polymer is poly(lactide-co-glycolide) (PLG), the first polynucleotide-containing species encodes for an antigen derived from a pathogenic organism such as HIV, the microparticles further comprise an adsorbed immunological adjuvant such as CpG and can contain 01-10wt% cationic surfactant (claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26, 29, 30, 34-37, 69, 76-79, 86, and 90, 91, and 96-100), **(ii)** a method of producing the microparticles by obtaining a w/o/w emulsion comprising the polymer and the surfactant, removing the organic solvent from the solution and adsorbing the first polynucleotide-containing species to the microparticles (claims 52, 54, 55, 92-95, and 101), **(iii)** a method of delivering a therapeutic amount of polynucleotide to a host animal (claim 38), and **(iv)** a method of stimulating an immune response, wherein the immune response comprises a CTL immune response (claims 39, 42, 44-48).

The application claims recite a microparticle comprising a biodegradable polymer such as PLG, a cationic detergent, an immunological adjuvant and an antigen derived

from a pathogenic organism such as HIV, wherein both the immunological adjuvant and the antigen are adsorbed on the surface of the microparticle, wherein the biodegradable polymer is PLG, and wherein the microparticles are formulated into an injectable pharmaceutical composition (claims 1-5, 11, 30, 31, 40, 43, 45-47,58, 59, 70, and 71); the adjuvant comprises CpGs (claims 36 and 37). The specification discloses that the antigen can be a plasmid such as pCMV encoding gp120 and that the cationic surfactant can be CTAB (p. 1, paragraph 0002, p. 4-5, paragraph 0019, p. 7, paragraph 0037, p. 17, paragraph 0070, Example 7). With respect to the limitation of the size of the particles being between 200 nm and 20 μm, the specification discloses that the microparticles can have a diameter of 200 nm to 30μm. The specification also discloses that the polynucleotide can constitute 5% or 0.1 to 10% of the total weight of the microparticle (p. 8, column 1, paragraph 0091) and that the microparticles comprise 0.1-10% or 0.5-2 % or cationic surfactant, wherein microparticle can comprise 1% detergent relative to the biodegradable polymer, and that the microparticles are obtained without removal of the detergent after particle formation (p. 18-19, paragraph 0075).

The applicant's arguments are not new and were previously addressed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 32-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76-83, and 86-101 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Hagan et al. (U.S. Patent No. 6,884,435, of record), as evidenced by Thalhamer et al. (Endocrine Regulations, 2001, 35: 143-166).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

O'Hagan et al. teach a microparticle comprising a biodegradable polymer such as PLG, a cationic surfactant such as CTAB, and a polynucleotide adsorbed on the surface of the microparticle (claims 1-3, 5, 6, 90, and 100), wherein the microparticles have a diameter of 200 nm to 30 μm, wherein the polynucleotide constitutes at least 5% or 10% of the total weight of the microparticle, wherein the polynucleotide is a plasmid such as pCMV (i.e., comprising CpGs) and wherein the plasmid encodes an antigen derived from a pathogenic organism such as HIV gp120 (claims 1, 8-10, 12, 13, 15-18, 27, 28, 61, 69, 90, 91, and 100); the microparticle is formed in the presence of the cationic surfactant and the cationic surfactant is not removed after the formation of the

microparticle and contains at least 5% (claim 1) (Abstract, column 2, lines 37-67, column 3, lines 17-34, column 5, lines 1-5, 28-35, and 65-67, column 9, lines 5-15, column 11, lines 1-6, column 12, lines 6-19, column 14, lines 1-12, Examples 2 and 7). O'Hagan et al. teach that the microparticles can be formulated into an injectable pharmaceutical composition, wherein the pharmaceutical composition further comprises an adjuvant such as an aluminum salt and wherein the adjuvant is adsorbed on the microparticle (claims 23, 26, 34-37, 55, 76-79) (column 14, lines 36-67, column 15, lines 66 and 67). O'Hagan et al. also teach a method of producing the above microparticle by forming a w/o/w emulsion comprising the cationic surfactant and the biodegradable polymer at a weight to weight ratio of 0.01:1, followed by the removal of the organic solvent and the absorption of the polynucleotide (claims 52, 54, and 92-95) (column 13, lines 10-39). In addition to the above, O'Hagan et al. teach a method for raising an immune response by administering their microparticles to a human (claims 38, 39, and 45-48), wherein the immune response comprises a CTL response (claims 42 and 44) (column 4, lines 3-30, column 7, lines 25-35, column 8, lines 45-52). With respect to claims 27, 28, 91, and 93, O'Hagan et al. teach that the polynucleotide can constitute 0.1% to 10% of the total weight of the microparticle (column 14, lines 8 and 9); the value of 10% is the same as the claimed lower point of the claimed range, and therefore, O'Hagan et al. anticipate the range 10% to 20% or 10% to 30% recited in claims 27, 28, 91, and 93. With respect to the limitation of the microparticle comprising 0.1 to 10 wt% cationic surfactant (claim 96), O'Hagan et al. teach a weight to weight ratio of cationic surfactant to polymer of 0.001:1, i.e., the microparticle comprises 0.1% cationic

surfactant (column 13, lines 30-37). With respect to the limitation of the microparticles comprising 0.5 to 2 % cationic surfactant (claims 97 and 101), O'Hagan et al. teach a weight to weight ratio of cationic surfactant to polymer of 0.005 to 1, i.e., the microparticle comprises 0.5% cationic surfactant (column 13, lines 30-37). With respect to the limitations recited in claims 98 and 99, O'Hagan et al. teach a ratio of cationic surfactant to biodegradable polymer of 0.01:1, i.e., the amount of surfactant is 1% relative to the biodegradable polymer (column 13, lines 30-37). With respect to the limitation recited in claims 56, 63, 64, and 86, O'Hagan et al. teach that the microparticle composition can comprise additional microparticles with the adjuvant adsorbed on their surface (column 14, lines 35-51); with respect to the limitation of the microparticles further comprising an immunological adjuvant (claim 64), it is noted that the microparticles of O'Hagan et al. comprising adsorbed plasmid contain CpGs, i.e., they further contain an immunological adjuvant. With respect to the limitations recited in claim 57, O'Hagan et al. teach that the microparticle composition can comprise additional microparticles with entrapped adjuvant (column 14, lines 35-51). With respect to the limitation of microparticle eliciting a Th1 response (claim 43), it is noted that this is an inherent property of CpGs (see Thalhamer et al., p. 145, column 2); since the microparticles of O'Hagan et al. comprise CpGs, they must necessarily induce a Th1 immune response.

Since O'Hagan et al. teach all the claim limitations, the claimed invention is anticipated by the above-cited art.

The applicant's arguments are the same and were previously addressed.

It is noted that the applicant argues that the passage from MPEP 2123 cited by the examiner is relevant for 103(a) and not 102 rejections because the quoted law involves rejections under 103 and not 102. In response, it is noted that such does not take away from the fact that the specification of O'Hagan et al. anticipates the claimed invention.

The applicant argues that the examiner chose to ignore case laws relevant to 102 rejections in favor of case laws which are on point only for 103(a) rejections. In response, it is noted that the examiner did not "chose to ignore" the case law presented by the applicant. The examiner clearly considered the case and explained more than one time why the instant invention is different from case law.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633